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Case Report

Warthin like Variant of Papillary Thyroid Carcinoma: A Rare Variant

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Abstract

Introduction: Warthin like papillary thyroid carcinoma is a rare variant that bears features similar to Warthin tumour of salivary gland. It shows papillary or follicular structures lined by oncocytic cells having typical nuclear features of papillary thyroid carcinoma and marked lymphoplasmacytic infiltrate in the stroma. *Case Report:* A 60 year old lady presented in the ENT OPD with right sided neck swelling since 2 years. On examination the swelling was firm, non-tender, moving with deglutition and measured 4x3 cm. FNA smears of the swelling were highly cellular and comprised of cells arranged in papillary clusters. The cells were predominantly oncocytic and showed nuclear grooving and intranuclear inclusions. Cytological diagnosis of papillary thyroid carcinoma (Bethesda Category VI) was offered. Thyroidectomy specimen measured 6.5x5x3 cm and right lobe revealed gray tan tumor with numerous papillae and few cystic areas. Microscopy revealed a well circumscribed tumour, with tumour cells arranged in papillary architecture with presence of dense lymphoplasmacytic infiltrate in the stalks of papillae. The cells lining the papillae had abundant granular eosinophilic cytoplasm and many of the cells showed nuclear grooving and intranuclear inclusions. Occasional psammoma bodies were also seen. The surrounding thyroid showed features of hashimoto's thyroidtis. A final diagnosis of Warthin like variant of papillary thyroid carcinoma was given. *Conclusion:* Warthin like variants of papillary thyroid carcinoma was given to papillary thyroid carcinoma, warranting a proper identification.

Keywords: Warthin-like variant, papillary thyroid carcinoma, Hashimoto's thyroiditis, salivary gland, thyroid.

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INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most frequently encountered thyroid malignancy. Many histological variants of PTC have been described in WHO endocrine 2017, including papillary microcarcinoma, encapsulated, follicular, diffuse sclerosing, tall cell, columnar, cribriform-morular, papillary hobnail. thyroid carcinoma with fibromatosis/fascitis like stroma, solid/trabecular. oncocytic, spindle cell, clear cell and Warthin like variant [1]. Tall cell, columnar and hobnail variants have a poorer prognosis compared to other variants of PTC [2, 3]. Warthin like variant of papillary thyroid carcinoma (WLPTC) is quite rare and a relatively newer entity that is known to have a better clinical outcome as that of conventional PTC. It is named so because it resembles Warthin tumor of salivary gland in view of presence of papillae lined by oncocytic cells and dense lymphoplasmacytic infiltrate in the papillary cores besides having classical nuclear features of PTC [4]. Herein, we present a rare case of WLPTC.

CASE REPORT

A 60 year old lady came to ENT OPD with right sided neck swelling for 2 years which was rapidly increasing in size for last 1 month. Physical examination revealed swelling in the right lobe of thyroid which was firm, non-tender, measuring 4x3 cm and moving with deglutition. Left lobe and isthmus of thyroid did not reveal any palpable lesion. No cervical lymphadenopathy was identified. Thyroid function tests were within normal limits. Clinical suspicion of malignancy was raised and ultrasonography (USG) and fine needle aspiration (FNA) were advised. USG neck showed single heterogeneously hypoechoic nodule in the right lobe of thyroid with complete peripheral halo and ill-defined margins. The case was reported as suspicious of thyroid malignancy (TI-RADS 4).

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FNA smears were highly cellular and comprised of follicular epithelial cells arranged in papillary clusters. The cells were predominantly oncocytic and nuclei showed presence of nuclear grooves and intranuclear inclusions. Few lymphocytes were also identified in the background. (Figure 1) The case was cytologically diagnosed as papillary thyroid carcinoma (Bethesda Category VI). Following this, patient underwent total thyroidectomy and specimen was sent for histopathological examination. On gross examination, right lobe of thyroid measured 5x3x3 cm, left lobe measured 4.5x1.4x2 cm and isthmus measured 1x0.4 cm. Cut section of right lobe showed a gray white to gray tan tumor measuring 4.5 x3x 1.7 cm with presence of numerous papillary structures and few cystic spaces.(Figure 2)The tumor was 0.3 mm away from isthmus. Left lobe of thyroid and isthmus were grossly unremarkable.



Fig-1

(A): Cytology smears showing tumor cells arranged in fragments with anatomical borders. (Papanicolaou stain: 100 x)(B) Follicular cells with oncocytic change and lymphocytic infiltration. (Giemsa: 400 x)

(C) Follicular cells with vesicular chromatin, moderate cytoplasm, and an occasional intranuclear inclusion (arrow). (Papanicolaou stain : 100 x)



Fig-2: Cut section of thyroid showing solid cystic areas with numerous papillae

On microscopy, tumor cells were arranged in papillary architecture and cells lining papillae had abundant eosinophilic granular cytoplasm oncocytic change). The papillary cores and the stroma of the tumor showed marked lymphoplasmacytic infiltrate. The nuclei were optically clear and displayed nuclear grooves and intranuclear inclusions. Occasional psammoma bodies were also noticed. Surrounding nonneoplastic thyroid tissue showed features of hashimoto's thyroiditis.(Figure 3) Based upon histopathological features simulating Warthin tumor of salivary gland and nuclear features of PTC, a final diagnosis of WLPTC was given. The patient is on follow up for 6 months and is doing well.



Fig-3:

(A) Tumor mass showing papillary architecture with dense lymphoplasmacytic infiltrate (Hematoxylin & eosin stain: 100 x)
(B) Papillae lined by oncocytic cells and showing nuclear features of PTC like chromatin clearing, intranuclear inclusion (yellow arrow) and nuclear groove (black arrow) (Hematoxylin & eosin stain: 400 x)
(C) Tumor mass with presence of psammoma bodies (arrow). (Hematoxylin & eosin stain: 400 x)
(D) Peritumoral thyroid tissue showing features of Hashimoto's thyroiditis. (Hematoxylin & eosin stain: 400 x)

DISCUSSION

WLPTC was first described in a series of 13 cases in 1995 by Apel *et al.* [5]. The important histological features that were used to diagnose WLPTC included: papillary architecture, oncocytic change, nuclear features of PTC and dense lymphoid infiltrates in papillary areas [5, 6]. Some authors consider WLPTC to be a subtype of oncocytic variant of PTC however, as per WHO Endocrine 2017, now it is a distinct entity [1, 2].

WLPTC is more commonly seen in females like other variants of PTC. The usual age of presentation of WLPTC is usually a decade earlier than that of conventional PTC with highest prevalence in the fourth decade [7]. However, in the present case the patient was 60 years old. BRAF and RET mutations known to occur in conventional PTC are also the most frequently encountered mutations in WLPTC, thus implicating that WLPTC is indeed a variant of PTC [7]. WLPTC is a quite rare variant of PTC accounting for only 0.2-1.9% of total PTC cases [8].

Precise cytological diagnosis of this variant is difficult as its findings are similar to conventional PTC (papillary clusters, nuclear grooves and intra nuclear cytoplasmic inclusions) and hashimoto's thyroiditis (lymphocyte rich background) [9]. Cytological features of WLPTC were first described by Youseff et al. in 1997, which included papillary clusters or monolayered sheets of hurthle (oncocytic) cells with nuclear features of PTC and dense lymphoid cell population in the background [8, 9]. Thus, the presence of predominantly oncocytic cells in papillary clusters showing nuclear features of PTC along with lymphoplasmacytic cells in background should raise a suspicion of WLPTC as was seen in the present case. However, based on these features also, it may be difficult to diagnose WLPTC on cytology as many a times conventional PTC arises in a background of Hashimoto's Thyroiditis.

WLPTC are usually circumscribed tumors seen in the form of grayish white nodule. Occasional cystic and hemorrhagic areas may be noticed like in our case few cystic areas were identified. The greatest dimension of tumor in the present case was 4.5cm which is in accordance with the tumor size of WLPTC (0.3-5.0 cm) reported in literature [6]. The tumor resembles Warthin tumor of salivary gland microscopically showing presence of papillary structures lined by oncocytic cells with prominent lymphoplasmacytic infiltrate in the papillary cores. The nuclear features similar to conventional PTC are also seen [6, 7].

Oncocytic changes can be seen in many benign and malignant lesions of thyroid like hashimoto's thyroiditis, nodular goiter with prominent oncocytic cells, medullary carcinoma with oncocytic cells, oncocytic variant of PTC, hurthle cell carcinoma and tall cell variant of PTC [6-8]. The common differential diagnosis of WLPTC include- conventional PTC with focal oncocytic change, conventional PTC with hashimoto's thyroiditis and tall cell and oncocytic variant of PTC. In hashimoto's thyroiditis papillae are rarely seen and only few nuclei show grooving [10]. Conventional PTC with focal oncocytic change as the name suggests have only focal oncocytic cells and lack dense lymphoplasmacytic infiltrate in the papillary cores or stroma.(11) The tumor cells in conventional PTC with hashimoto's thyroiditis usually do not show overt oncocytic change in the cells lining the papillae and lymphoplasmacytic infiltrate in papillary cores [6] Oncocytic cells can be seen in both tall cell variant and oncocytic variant of PTC but the cases to be diagnosed as tall cell variant of PTC must fulfil the criteria of having oncocytic cells that are two to three times as tall as they are wide and such tall cells must comprise >30% of all tumor cells. Tall cell variant usually lacks the presence of lymphoplasmacytic infiltrate in the stroma [1]. The oncocytic variant of PTC in its pure form is rare, and consists of often encapsulated, invasive, papillary tumors having oncocytic cell cytology throughout [1]. But oncocytic variant also shows absence of lymphocytic infiltrate seen in WLPTC [1, 11]. Differentiating these 2 variants from WLPTC is necessary as they have poorer prognosis and require aggressive therapy and close follow up in comparison to WLPTC [1, 10, 11]. Thus, identifying the correct histomorphology is critical as some of the mimickers of WLPTC have more aggressive and unfavourable outcomes.

A close association between Hashimoto's thyroiditis and PTC was first observed by Dailey *et al.* in 1995 [12]. Coexistence of PTC with hashimoto's thyroiditis is 2.8 times more common than in other types of thyroid carcinoma [7, 13]. Similarly, various reports suggest that WLPTC is also commonly accompanied by hashimoto's thyroiditis in background as seen in our case [8, 14]. WLPTC is known to be associated with better prognosis as it has lower rate of lymph node metastases, vascular invasion, capsular invasion, extrathyroidal extension, TNM staging and lower frequency of BRAFV600E mutations [4, 6]. This favorable prognosis is mainly attributed to the presence

of lymphoid tissue within the tumor. It has been hypothesized that lymphocytic infiltration in non-tumor bearing thyroid tissue is activated through autoimmune mechanism by presence of RET/PTC fusion gene of PTC [11]. The lymphocytic and plasma cell infiltration seen also serve as host immune response to tumor [12, 14].

Total thyroidectomy with/without lymph node dissection is the treatment modality depending upon the tumour stage at the time of diagnosis [9]. The present case is being reported because of the rare occurrence of this entity as well as to focus on the problems in the preoperative cytological diagnosis of this rare variant of PTC.

CONCLUSION

WLPTC is an uncommon variant of PTC that is now acknowledged as a distinct entity with an excellent prognosis. Although histopathology remains the cornerstone for diagnosing WLPTC but presence of predominantly oncocytic cells in papillary clusters showing nuclear features of PTC along with lymphoplasmacytic cells in background on cytology smears should raise a suspicion about WLPTC. The correct diagnosis of this entity will help in better patient management and outcome.

REFERENCES

- 1. Tallini, G., Biase, D. D., Repaci, A., & Visani, M. (2019). What's new in thyroid tumor classification, the 2017 World Health Organization classification of tumours of endocrine organs. In *Thyroid FNA Cytology* (pp. 37-47). Springer, Singapore.
- Lloyd, R. V., Buehler, D., & Khanafshar, E. (2011). Papillary thyroid carcinoma variants. *Head and neck pathology*, 5(1), 51-56.
- 3. Lam, A. K. Y., Lo, C. Y., & Lam, K. S. L. (2005). Papillary carcinoma of thyroid: a 30-yr clinicopathological review of the histological variants. *Endocrine pathology*, *16*(4), 323-330.
- Paliogiannis, P., Attene, F., Trogu, F., & Trignano, M. (2012). Warthin-like papillary carcinoma of the thyroid gland: case report and review of the literature. *Case Reports in Oncological Medicine*, 2012.
- Apel, R. L., Asa, S. L., & LiVolsi, V. A. (1995). Papillary Hürthle cell carcinoma with lymphocytic stroma." Warthin-like tumor" of the thyroid. *The American journal of surgical pathology*, 19(7), 810-814.
- Sahoo, P. K., Patnayak, R., Khan, P. A., & Jena, A. (2020). Warthin-like variant of Papillary thyroid carcinoma—Case report of an uncommon tumour with review of literature. *International Journal of Surgery Case Reports*, 77, 9-11.
- Wajahat, M., Jeelani, T., Gupta, K., & Bashir, N. (2018). Warthin like papillary carcinoma-a rare

variant of papillary carcinoma thyroid. Human Pathology: Case Reports, 13, 21-23.

- Kumar, T., Nigam, J. S., Tewari, P., & Jha, C. K. (2020). Warthin-like variant of papillary thyroid carcinoma: an uncommon variant. *Cureus*, 12(12).
- Kim, J., Lim, B. J., Hong, S. W., & Pyo, J. Y. (2018). Preoperative cytologic diagnosis of warthin-like variant of papillary thyroid carcinoma. *Journal of Pathology and Translational Medicine*, 52(2), 105.
- Goldblum, J.R., Lamps, L.W., McKenney, Myers, J.L. (2011). Thyroid gland. Rosai and Ackermans Surgical Pathology.10th edition. Philadelphia: Elsevier, 492–493.
- D'antonio, A., De Chiara, A., Santoro, M., Chiappetta, G., & Losito, N. S. (2000). Warthinlike tumour of the thyroid gland: RET/PTC

expression indicates it is a variant of papillary carcinoma. *Histopathology*, *36*(6), 493-498.

- 12. DAILEY, M. E., LINDSAY, S., & SKAHEN, R. (1955). Relation of thyroid neoplasms to Hashimoto disease of the thyroid gland. *AMA archives of surgery*, 70(2), 291-297.
- Konturek, A., Barczyński, M., Wierzchowski, W., Stopa, M., & Nowak, W. (2013). Coexistence of papillary thyroid cancer with Hashimoto thyroiditis. *Langenbeck's archives of surgery*, 398(3), 389-394.
- 14. Mishra, A., Jayalakshmi, V., Chaturvedi, U. P., Chikhale, N. P., Patel, R. D., & Cherian, S. (2013). Oncocytic variant of papillary thyroid carcinoma and associated lymphocytic thyroiditis: A case report with review of literature. *Int J Head Neck Surg*, *4*, 89-91.